

complement components in dermatitis herpetiformis was not affected by dapsone therapy.⁷

The beneficial effect of dapsone in cutaneous vasculitis and in dermatitis herpetiformis can be explained by its direct action on the myeloperoxidase-H₂O₂-halide mediated cytotoxic systems in the polymorphonuclear leucocyte, and evidence that it inhibits the alternative pathway of complement activation is lacking.

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SOFT TISSUE SARCOMAS AND CHLORINATED PHENOLS

SIR,—Whilst it is important to record soft tissue malignancies in those who have been exposed to 2,4,5-T based herbicides (since those based on 2,4-D have a clean bill of health in this respect), data such as those of Dr Johnson and colleagues (July 4, p. 40) only confuse further an already difficult situation. One patient had a "short exposure" (how short?) and the other "prolonged exposure" (how long?). What were the chemicals and what was the contact with them? If these questions are not answered in such reports, however brief, the search for truth is hampered. Animals receiving 2,4,5-trichlorophenoxyacetic acid based herbicides have not developed tumours—only those given chlorinated dioxins have done so.

Allen's unsatisfactory experiments² showed soft tissue malignancies in rats, but in their much more reliable studies Kociba³ and Holmes⁴ recorded only epithelial malignancies in rats and mice receiving hexachloro (HCDD) and tetrachloro (TCDD) dioxin daily throughout their lifetimes.

This letter does not seek in any way to discourage these most necessary reports—only to put forward a plea for more detailed and correct information to make them more meaningful.

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NON-HODGKIN'S LYMPHOMA OF THE SCALP IN WORKERS EXPOSED TO DIOXINS

SIR,—Dr Hardell and Dr Eriksson (Aug. 1, p. 250) refer to their studies of soft-tissue sarcomas in Swedish lumberjacks and to the seven cases of such sarcomas in workers in the U.S. chemical industry which have been recorded in *The Lancet* this year. During the past 5 years we have been concerned with a plant which until 1978 manufactured pentachlorophenol and its sodium salt. Homologues of "dioxin" (TCDD), particularly the hexachloro and octachloro dibenzodioxins, occurred as contaminants up to about 300 p.p.m. at the intermediate stages of manufacture and 5 p.p.m. in the final products. Cases of chloracne, mostly mild, some moderate and a very few severe, occurred among the 158 operatives. Since 1978, 2 cases of non-Hodgkin's lymphoma in the skin have developed among people who had worked on this process.

The first patient is now aged 74 and was involved in pentachlorophenol manufacture from 1959 to 1972. A tumour in the scalp developed in 1976, the histology of which was described as follows: "The sections show diffuse infiltration of the dermis and

subcutaneous tissue with lymphoid cells. The histology suggests a non-Hodgkin's lymphoma composed of moderately well differentiated lymphoid cells. The predominant cells are cleaved lymphocytes perhaps indicating that the original lymphoma might have shown a nodular pattern." He also had mild chloracne of the face and trunk.

The second patient is 56. He was employed as an operator on the same plant as the first case from 1957 to 1978. He had severe chloracne of the face, neck, trunk, and genitals. In 1978 a tumour developed in the right occipital region of the scalp, described as a non-Hodgkin's lymphoma. The detailed histology was as follows: "Histology showed a malignant lymphoma which is partially follicular and partially diffuse of predominantly large cell (centroblastic) type. The appearances indicate a follicular lymphoma at the most poorly differentiated end of the range."

Both these men had worked on processes in these works involving exposure to other chemicals including aromatic hydrocarbons, among them benzene.

The number of neoplasms of this type (ICD 200 and 202) to be expected in this group of 158 workers is 0.28. If ICD 200 alone is considered, the expected number is 0.2.

We thank Prof. E. Wilson Jones (Institute of Dermatology, London) and Dr J. Gough (Welsh National School of Medicine) for descriptions of the histology in the first and second case, respectively, and Dr R. D. Jones (Employment Medical Advisory Service Headquarters) for advice on epidemiological aspects.

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ASTHMA DEATHS AND THEOPHYLLINE/BETA₂-AGONIST THERAPY

SIR,—We are alarmed by the report from Dr Wilson and colleagues (June 6, p. 1235) of a sharp increase in asthma deaths in New Zealand, especially among young people, and by their suggestion that it might be linked to increased prescribing of theophylline along with beta₂-adrenergic agents. Subsequent correspondents (July 4 and 25) offer some contrary opinions and a few useful further facts. Since we have been studying the interaction between these drugs in patients with asthma and bronchitis for some years and have had no hint, either in the laboratory or the clinic, that the combination is dangerous, we feel the need to examine Wilson's arguments in more detail. We do not think that their data support their primary conclusion that the death rate is suddenly rising; nor do published data or our own observations support their speculation that the combination may cause cardiac deaths.

Analysis of Wilson and colleagues' death rate data, as corrected by Dr Beaglehole and colleagues (July 4, p. 38), shows a highly significant least squares linear correlation ($r^2 = 0.972$; $p < 0.002$), the annual death rate rising by $17.8 (\pm 1.8 \text{ SD})$ each year over 1974–8. The 240 annual total deaths, extrapolated from the 20 in 4 months in Auckland—the experience which alarmed Wilson et al.—is not outside the expectation based on these earlier years. Similarly, their collection of 8 cases under the age of 25 between May 30, 1980, and Feb. 5, 1981, does not seem outside the New Zealand average of 25 ± 11.6 over these earlier years for the under 25 age group. This further analysis confirms Dr Whittington's view (July 4, p. 37) that their numbers do not justify their alarm.

Their anecdotal data are no better. We cannot accept that death after beta-blocker eye drops (case 1) can be attributed to salbutamol therapy, nor can we accept a death as due to theophylline overdose (case 2) without a plasma level, or at least sufficient information about dosage to allow its approximate calculation.

Extensive published work shows nothing to suggest that these

2. Allen J, Van Miller JP. Chronic toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rats. *Fed Proc* 1977; 36: 673.

3. Kociba RJ, Keys DG, Beyer JE, Carreon RM, Wade CE, Dittenber DA, Kalnins RP, Franson LE, Park CN, Barnard SD, Hummel RA, Humiston CG. Results of 2 years chronic and oncogenicity study of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rats. *Toxicol Appl Pharmacol* 1978; 46: 279–303.

4. Holmes PA, Russ JH, Richter WR, Sheffer AM. Long term effects of TCDD and HCDD in mice and rats. In: New York Academy of Sciences, science week June 21–30, 1978: abstr 26.

1. Snodgrass W, Sawyer D, Conner CS, Rumbach BH, Peterson RG, Sullivan JB Jr. Asymptomatic theophylline overdose. *Drug Intel Clin Pharmacol* 1980; 14: 783–85.